

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: J. Rine et al. Attorney Docket No.: UOCB118456  
Application No.: 10/038,206 Art Unit: 1631 / Confirmation No: 1317  
Filed: January 2, 2002 Examiner: J.S. Brusca  
Title: SYSTEMS FOR GENERATING AND ANALYZING  
STIMULUS-RESPONSE OUTPUT SIGNAL MATRICES

APPELLANTS' REPLY BRIEF

Seattle, Washington 98101

September 28, 2007

TO THE COMMISSIONER FOR PATENTS:

This brief is being filed in accordance with 37 C.F.R. § 41.41(a) and in response to an Examiner's Answer mailed on July 31, 2007.

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## STATUS OF CLAIMS

Claims 38-85 are pending in the application. All stand rejected under 35 U.S.C. § 103(a).

Claims 38-85 are appealed. The table below indicates their status.

<b>Claim(s)</b>	<b>Status</b>	<b>Appealed</b>
1-37	Canceled	No
38	Rejected	Yes
39	Rejected	Yes
40	Rejected	Yes
41	Rejected	Yes
42	Rejected	Yes
43	Rejected	Yes
44	Rejected	Yes
45	Rejected	Yes
46	Rejected	Yes
47	Rejected	Yes
48	Rejected	Yes
49	Rejected	Yes
50	Rejected	Yes
51	Rejected	Yes
52	Rejected	Yes
53	Rejected	Yes
54	Rejected	Yes
55	Rejected	Yes
56	Rejected	Yes
57	Rejected	Yes
58	Rejected	Yes
59	Rejected	Yes
60	Rejected	Yes
61	Rejected	Yes
62	Rejected	Yes
63	Rejected	Yes
64	Rejected	Yes
65	Rejected	Yes
66	Rejected	Yes
67	Rejected	Yes
68	Rejected	Yes
69	Rejected	Yes

<b>Claim(s)</b>	<b>Status</b>	<b>Appealed</b>
70	Rejected	Yes
71	Rejected	Yes
72	Rejected	Yes
73	Rejected	Yes
74	Rejected	Yes
75	Rejected	Yes
76	Rejected	Yes
77	Rejected	Yes
78	Rejected	Yes
79	Rejected	Yes
80	Rejected	Yes
81	Rejected	Yes
82	Rejected	Yes
83	Rejected	Yes
84	Rejected	Yes
85	Rejected	Yes

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## GROUND OF REJECTION TO BE REVIEWED ON APPEAL

### First Ground of Rejection - Claims 38-53, 55-66, 68-83, and 85

Claims 38-53, 55-66, 68-83, and 85 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gress et al. (*Mammalian Genome* 3:609-619, 1992), in view of Granelli-Piperno et al. (*J. Exp. Med.* 163:922-937, 1986), in view of either Fodor et al., 1998 (U.S. Patent No. 5,800,992), or Fodor et al., 1991.

### Second Ground of Rejection - Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84

Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gress et al., in view of Granelli-Piperno et al., in view of either Fodor et al. 1998 or Fodor et al. 1991, as applied to Claims 38-53, 55-66, 68-83, and 85 above, and further in view of Watson et al. (*Molecular Biology of the Gene*, 4th ed., Benjamin Cummings, Menlo Park, 1987, pp. 550-594).

## ARGUMENT

The Rejection of Claims 38-53, 55-66, 68-83, and 85 Under 35 U.S.C. § 103(a) as Being Allegedly Unpatentable Over Gress et al. in View of Granelli-Piperno et al. in View of Either U.S. Patent No. 5,800,992 (Fodor et al. '98) or Fodor et al. 1991

Appellants maintain the position that a *prima facie* case of obviousness has not been established because (1) there is no motivation to modify Gress et al. as proposed by the Examiner; rather, Gress et al. actually teaches away from the present invention; (2) the modification of Gress et al. with predetermined sequences made by the methods disclosed by Fodor et al. '98 or '91, as proposed by the Examiner, would render the method of Gress et al. inoperable for its intended purpose; (3) impermissible hindsight reconstruction has been used to improperly combine elements from Gress et al. and Fodor et al. '98 or '91; and (4) even if improperly combined, the teachings of Granelli-Piperno et al. and either Fodor et al. '98 or Fodor et al. '91 fail to cure the deficiencies of Gress et al. because the combined teachings do not teach or suggest all the claim limitations.

### *Gress et al. Teaches Away from the Claimed Invention*

As an initial matter, appellants note that the Examiner has mischaracterized the teachings of Gress et al. in the Examiner's Answer mailed on July 31, 2007. In the Examiner's Answer, the Examiner has taken the position that it would have been obvious to modify the method of Gress et al. by assaying cells that have received treatments with different drugs according to the method of Granelli-Piperno et al. because "the method of Gress et al. in which the *treated cell cDNA* is applied to an array of probes is an improvement over the assay method of Granelli-Piperno et al. in which a single gene is applied to RNA from the treated cell that is on a membrane because it allows for simultaneous assay of a large number of genes for effects of the drug on gene expression." See page 6 of Examiner's Answer (emphasis added). Contrary to the

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Examiner's assertion, Gress et al. is directed to identification of previously uncharacterized highly expressed transcripts and does not teach or suggest the use of cDNA from *treated* cells.

In response to appellants' arguments that Gress et al. teaches away from the claimed invention, the Examiner maintains the position that Gress et al. shows "that despite the necessity of controls it is possible to quantify levels of gene expression by their method, as shown in figure 2 and Table 1." Examiner's Answer, page 8. Appellants disagree with the Examiner's conclusion. As previously noted, Figure 2 of Gress et al. merely shows the identification of positive versus negative clones (see Appeal Brief, pages 15-16). Moreover, the Examiner has not addressed the issue of quantitative measurement for *same-species* analysis, as required in the claimed method. In this regard, it is noted that Table 1 of Gress et al. demonstrates that the Gress et al. method is not suitable for *same-species* analysis due to the high background hybridization resulting from repetitive sequences (see page 14 of the Appeal Brief).

Therefore, because Gress et al. teaches away from the claimed invention, one of skill in the art would not have a reasonable expectation of success to modify the method of Gress et al. by assaying cells that have received treatments with different drugs according to the method of Granelli-Piperno et al., as suggested by the Examiner. As recently reaffirmed by the Supreme Court, "when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740, 82 U.S.P.Q.2d 1385, 1395 (2007).

*Modification of Gress et al. With Predetermined Sequences as Disclosed by Fodor et al. '98 or '91 Would Defeat the Intended Purpose of Gress et al.*

Appellants maintain the position that the modification of Gress et al. with predetermined sequences disclosed by Fodor et al. would render Gress et al. inoperable for its intended purpose of gene discovery. It is well established that if a proposed modification would render a prior art

invention being modified unsatisfactory for its *intended purpose*, then there is no suggestion or motivation to make the proposed modification. *See In re Gordon*, 733 F.2d 900, 221 U.S.P.Q. 1125 (Fed. Cir. 1984); M.P.E.P. 2143.01(V).

In response to appellants' argument that Fodor et al. '91 is not combinable with Gress et al. because the use of predetermined sequences of probes shown in Fodor et al. '91 would make Gress et al. inoperable for its intended purpose, the Examiner asserts that "the use of predetermined sequences of probes allows for use of the array of Gress et al. for *additional purposes*...[t]he modification of the array of Gress et al. by use of predetermined sequences of probes *does not conflict with the purpose of Gress et al.* of using the array for identification of highly expressed cDNA clones." Examiner's Answer at page 8 (emphasis added).

Contrary to the Examiner's assertion, appellants maintain the position that modification of the Gress et al. method to replace the thousands of unidentified cDNA clones arrayed on a substrate with thousands of probes which each have a pre-determined sequence would only permit an investigator to identify the expression pattern of those clones in the pool that happen to hybridize to one of the pre-determined sequences, which would *defeat the intended purpose* of Gress et al. which was *gene discovery* (see Appeal Brief at pages 18-20).

*Impermissible Hindsight Reconstruction Has Been Used to Improperly Combine Elements From Gress et al. and Fodor et al. '98 or '91*

Appellants maintain the position that the Examiner has applied improper hindsight analysis by using the claimed invention as a template in attempting to piece together isolated disclosures of prior art in an assertion that the claimed invention is obvious. As previously pointed out by appellants, the purpose and focus of the Gress et al. and Fodor et al. publications are quite different, and there is no motivation to combine them, or to select individual elements

of the disclosure of each of these publication and combine them in the manner claimed. See page 21 of the Appeal Brief.

Further in this regard, in *KSR*, the Supreme Court reaffirmed the dangers of hindsight bias, and warned against arguments based upon *ex post* reasoning. *KSR*, 127 S. Ct. at 1742 (citing *Graham v. John Deere Co.*, 383 U.S. 1, 36 (1966) (warning against a "temptation to read into the prior art the teachings of the invention in issue" and instructing courts to "guard against slipping into the use of hindsight") (internal quotations omitted)). See also U.S.P.T.O. *KSR* Memorandum, May 3, 2007 ("in formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed").

Moreover, as described above, because Gress et al. teaches away from the claimed invention, there is no expectation of success and therefore no motivation to modify Gress et al. as suggested by the Examiner.

*Even if Improperly Combined, the Combined Teachings Do Not Teach or Suggest All the Claim Limitations*

To establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art. M.P.E.P. 2143.03. However, it is noted that the Examiner has not addressed appellants' argument that even if combined, none of the cited references teach or suggest the step of storing in digital form each electrical output signal in an output signal data structure, wherein each stored digital signal is associated (i) with said stimulus; and (ii) with the identity of said identified gene. See Appeal Brief at page 24.

Consequently, appellants maintain the position that the subject matter of Claims 38-53, 55-66, 68-83, and 85 is not obvious in view of the teachings of Gress et al. in view of Granelli-



Piperno et al. in view of either U.S. Patent No. 5,800,992 (Fodor et al. '98) or Fodor et al. 1991. Reversal of this ground of rejection is respectfully requested.

The Rejection of Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 Under 35 U.S.C. § 103(a) as Being Allegedly Unpatentable Over Gress et al. in View of Granelli-Piperno et al. in View of Either U.S. Patent No. 5,800,992 (Fodor et al. '98) or Fodor et al. 1991, and Further in View of Watson et al.


For at least the reasons set forth *supra* in connection with the rejection of Claims 38-53, 55-66, 68-83, and 85 under 35 U.S.C. § 103(a), it is submitted that it is not obvious to combine the teachings of Gress et al., Granelli-Piperno et al., or Fodor et al., as suggested by the Examiner. As previously pointed out by the appellants, this deficiency is not cured by the teachings of Watson et al. Appeal Brief at page 25. Consequently, appellants respectfully request reversal of the Examiner's rejection of Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 under 35 U.S.C. § 103(a).

#### CONCLUSION

For at least the foregoing reasons, appellants respectfully submit that Claims 38-85 are in condition for allowance. Accordingly, appellants request reversal of the rejections of Claims 38-85 under 35 U.S.C. § 103(a).

Respectfully submitted,

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